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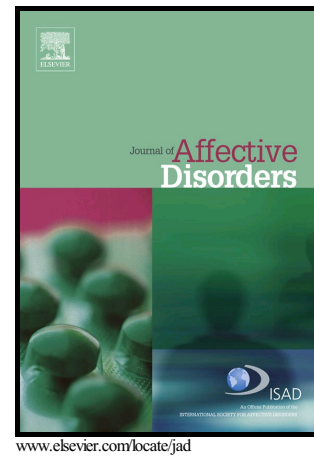
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Influences of the Big Five personality traits on the treatment response and longitudinal course of depression in patients with acute coronary syndrome: A randomised controlled trial

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Abstract

Background

Influences of the Big Five personality traits on the treatment response and longitudinal course of depression in patients with acute coronary syndrome: A randomised controlled trial.

Methods

This naturalistic observational study initially recruited 1,152 ACS patients; 685 patients completed personality assessments at baseline, of whom 630 were followed-up one year later. Of the 294 patients with depression, 207 participated in a 24-week double blind trial of escitalopram or placebo. The remaining 87 patients who received medical treatment only and the 391 who had not depression were also followed in a one year naturalistic observational study. The Big five personality traits were assessed using the Big Five Inventory. The

influences of personality on the Hamilton Depression Rating Scale score changes were analysed using a mixed-model repeated-measures analysis of covariance.

Results

A Cluster analysis identified two personality types: resilient and vulnerable. The vulnerable personality type was characterised by lower extraversion, agreeableness, and conscientiousness – but higher neuroticism – than the resilient type. This personality type was independently associated with a poorer outcome of depression in ACS patients during the 24-week treatment period and the one year longitudinal follow-up period compared to the resilient personality type, irrespective of treatment allocation.

Limitations

Recruitment from a single institution may limit generalisability. Personality traits were investigated 12-weeks after ACS; thus, the responses may have been influenced by the prior receipt of escitalopram.

Conclusions

Personality types influences the treatment outcome and longitudinal course of depression in ACS patients independent of antidepressant treatment.

Introduction

Depression is common in patients with acute coronary syndrome (ACS) (Rudisch and Numeroff, 2003). However, while the stress associated with this physical illnesses is likely to be an important factor, there are also likely to be variations in an individual's response to illness which may modify this outcome. Personality traits are key factors that can influence individual perceptions regarding illness-related stressors (Groves and Muskin, 2011). Several studies have attempted to define vulnerabilities to psychological or physical health

consequences following ACS, particularly the traditional type A behavior and D personality (Roseman et al., 1976; Denellot et al., 1995). Type A behavior is characterized by hostility, time urgency and competitiveness behavior patterns, and is a risk factor for cardiovascular disease (Roseman et al., 1976). However, most researches on type A behavior has focused on cardiovascular morbidity and mortality (Steptoe and Molloy, 2007) rather than depression in patients with heart disease. The type D personality is characterised by negative affectivity and social inhibition and is a risk factor for the development and persistence of depressive symptoms in cardiac patients (Denellot et al., 1995; Pedersen et al., 2006; Martens et al., 2008). However, there has been still debate on the potential overlap between negative affectivity and depression, and whether type D is a stable personality type or a response to an illness (Steptoe and Molloy, 2007; Marchesi et al., 2014). Furthermore, these personality types (A or D) represent limited and specific aspects of personality.

In contemporary psychology, the Five Factor Model (FFM) is the most accepted, widely used and comprehensive model of human personality (McCrae, 2001). The FFM consists of the following Big Five personality dimensions: extraversion, agreeableness, conscientiousness, neuroticism, and openness. Numerous studies have investigated the influences of FFM personality on the risk, treatment response and prognosis of depression in general populations (Kotov et al., 2010; Wardenaar et al., 2014; Bagby et al., 2008; Thibodeau et al., 2015). The FFM has also been used widely in depression in patients with chronic physical illness, mainly for risk investigation but also in a few studies of treatment response and longitudinal course (Aben et al., 2002; Westlake et al., 2005; de Jonge et al., 2006). Other than findings showing that neuroticism is associated with the risk of depression in patients with cardiac disease (Westlake et al., 2005; de Jonge et al., 2006; Duits et al., 1999), randomised trials investigating the influence of FFM personality traits on the risk of

depression and the course or treatment response in patients with ACS have yet to be conducted.

The FFM can be investigated either as five dimensions separately (a dimensional or variable-centered approach) or in combination (a typological or person-centered approach) (Costa et al., 2002; Asendorpf, 2002). From a clinical perspective, the typological approach provides a more integrative framework for personality and health assessment, and thus has drawn more attention recently (Asendorpf, 2002). The FFM typological approach has revealed that overcontrolled or vulnerable personality types are associated with an increased risk of, or poorer treatment outcomes for depression (Wardenaar et al., 2014; Asendorpf, 2002; Chapman and Goldberg, 2011). However, to the best of our knowledge, no studies have used the FFM typological approach to investigate depression in patients with ACS.

The aim of the study was to identify the influence of the Big Five personality traits on the treatment response and longitudinal course of depression in patients with ACS. The findings obtained using the typological approach are detailed in the main body of this manuscript due to their potential clinical utility, while the data obtained using the dimensional approach are described in the Supplementary materials.

Methods

Study overview and participants

This analysis was conducted using data from a large naturalistic study of patients with ACS, the Korean DEPression in ACS (K-DEPACS) study, which also included a nested randomised controlled trial for depressive patients with ACS, the Escitalopram for DEPression in ACS (EsDEPACS) study. Comprehensive study details and eligibility criteria for the K-DEPACS and EsDEPACS participants have been published (Kim et al., 2014).

The K-DEPACS study was carried out from 2006 to investigate the epidemiology of depression in ACS using a naturalistic prospective design. The participants were consecutively recruited from among patients recently hospitalised for ACS ($n = 4,809$) in the Department of Cardiology of Chonnam National University Hospital, Gwangju, South Korea. All patients were treated by the study cardiologists based on international guidelines for the management of ACS. Those who met the eligibility criteria and agreed to participate ($n = 1,152$) were assessed for depressive disorders. Following the ACS diagnosis, diagnoses of depressive disorders were determined using the Mini International Neuropsychiatric Interview (MINI) based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV). The MINI is a structured diagnostic psychiatric interview for the DSM-IV that can be used to diagnose major or minor depressive disorder (Sheehan et al., 1998). Using these criteria, patients were diagnosed with a major depressive disorder (MDD) if they had at least one core symptom of depression (e.g. depressed mood or loss of interest) along with at least four other symptoms. A diagnosis of a minor depressive disorder was made if a patient had at least one core symptom plus at least two, but less than four, of the other symptoms. In our study, the criterion for duration of symptoms was within rather than at least 2 weeks due to the particular study design at baseline. Of those, 446 were diagnosed with either major or minor depressive disorder; 300 of these patients agreed to be randomised to a 24-week, double-blind, placebo-controlled trial investigating the efficacy and safety of escitalopram; i.e. the EsDEPACS study. (ClinicalTrial.gov registry number: NCT00419471). The primary results of the EsDEPACS trial have been published, and showed that escitalopram was superior to placebo (Kim et al., 2015).

Personality was assessed 12-weeks after the baseline evaluation, then 685 (59.5%) received personality assessments and formed the sample for the analyses presented here. Of

the remaining 467 patients, 287 were lost to follow-up, 10 died, 120 refused to participate, and 50 were too unwell to participate on 12-weeks. Of the analysed group, 294 participants were diagnosed with either a major or minor depressive disorder and, of these patients, 207 agreed to participate in the EsDEPACS study. The remaining 87 patients who had depression but declined participation in the trial received conventional medical treatment for ACS only (MTO). All patients who participated in the K-DEPACS and EsDEPACS studies were contacted for follow-up investigation at one year after the baseline evaluation. Written informed consent was collected for the K-DEPACS and EsDEPACS studies, both of which were approved by the Chonnam National University Hospital Institutional Review Board.

Personality assessments

Personality was assessed by the Big Five Inventory (BFI), which was selected to represent the core traits in FFM personality (John and Srivastata, 1999). Terminology applied to these five traits has been described as follows: 'Extraversion' - talkative, assertive, and energetic; 'Agreeableness' - good-natured, cooperative, altruistic and empathic; 'Conscientiousness' - orderly, responsible, and dependable; 'Neuroticism' - neurotic, easily upset and not self confident; and 'Openness' - openness to experience, intellectual, imaginative, and independent-minded. Self-report ratings are made on a scale from 1 to 5 for each of 44 scale items, and higher scores represent higher levels of each given trait (John and Srivastata, 1999). The BFI has been translated and validated in Korean (Kim et al., 2010). Unfortunately a prospective design with pre-morbid personality was not possible in the present clinical setting; however, the BFI was performed 12-weeks after the baseline assessment to minimise the influence of the ACS and the reaction of patients to this diagnosis.

Using the typological approach, personality cluster was identified using cluster analysis.

Result of identical analyses with the two-step procedure specified by Asendorpf et al. (2001), two personality types were identified: resilient and vulnerable. Ward's hierarchical clustering procedure was applied for the initial solution; then, iterative k-means clustering, using Ward's method to define the initial cluster centres, was performed. Each case was assigned to a cluster based on the Euclidean distance from the cluster means; all data was z-standardised to determine the Euclidean distance. The largest shifts in cluster coefficients were observed in the transition from the two- to one-cluster solution; therefore, a two-cluster solution was accepted as the best initial solution. The cluster centres derived from the initial solution were used to implement non-hierarchical k-means clustering.

To evaluate the replicability of the final solutions, the method of Asendorpf et al. (2001) was used. Briefly, all cases were randomly split into halves and the full two-step procedure was applied to each half. Next, the participants from each half were assigned to new clusters according to the cluster centres of the other half of the sample. These new clusters were then compared to determine if they agreed with the original clusters according to Cohen's k . A kappa value > 0.60 was required as evidence of replication; the present results satisfied this criterion (replicability coefficients with Cohen's k : 0.833).

Compared with the second cluster, the first cluster was characterized by significantly higher extraversion, higher agreeableness, higher conscientiousness, but lower neuroticism (all $p < 0.001$). As defined and labeled in previous studies, the first cluster was labeled as resilient type and the second was vulnerable type (Wardenaar et al., 2014, De Fruyt, 2002). The personality profiles of the two clusters are shown in Fig. 1, with z scores used for ease of interpretation.

Outcomes

The primary efficacy outcome measure was change in score on the 17-item Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960) from baseline to endpoint. The HDRS was administered at baseline and 24-weeks for the EsDEPACS study, and at baseline and one year for the K-DEPACS study.

Demographic and clinical characteristics at baseline

Baseline characteristics evaluated included demographic and depression-related characteristics, cardiac risk factors, and current cardiac status. Demographic characteristics comprised age, gender, and duration of education. Baseline HDRS score and previous history of depression were evaluated for depression-related characteristics. Cardiac risk factors assessed comprised the following: self-reported diagnoses of hypertension or diabetes mellitus, hypercholesterolemia (fasting serum total cholesterol level >200mg/dl), obesity based on body mass index (BMI), self-reported current smoking status, previous history of ACS, and family history of ACS. In relation to cardiac status, diagnoses of myocardial infarction or unstable angina were distinguished, the severity of ACS was measured by the Killip classification (Killip and Kimball, 1967), left ventricular ejection fraction (LVEF) was estimated using echocardiography, and serum cardiac biomarkers troponin I and creatinine kinase-MB were measured.

Statistical analysis

Baseline characteristics were compared between the two personality types (resilient vs. vulnerable) by χ^2 or independent t tests. To identify the influence of the personality types on escitalopram treatment response in the EsDEPACS trial, the participants were divided into two groups, escitalopram vs. placebo, and mixed model repeated-measures analyses of

covariance (RMANCOVA) were used to assess interactions between time \times group, time \times personality type, and time \times group \times personality type. These variables were assessed in relation to the change in HDRS score at 24-weeks after adjusting for all covariates, including baseline HDRS score, previous depression, and previous history of ACS; a full model was used to avoid the risk of overfitting due to univariate pre-selection.

The influence of the personality types on the longitudinal course of depression was analysed, in the K-DEPACS participants who completed the one year follow-up assessment, after categorising the participants into four groups: no depression, depression on MTO, depression on escitalopram, and depression on placebo. Mixed model RMANCOVA was then performed to determine the associations of time \times group, time \times personality type, and time \times group \times personality type on one year HDRS score changes, after adjusting for all covariates. Additional subgroup analyses stratified by type of depression (major vs. minor) were conducted to identify the influences of personality type on treatment response at 24-weeks and one year. Additional analyses of dimensional FFM output were conducted; these are described in the Supplementary material. Statistical significance was set at $p < 0.05$ (two-sided), and all analyses were carried out using SPSS software version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

Recruitment

The flow chart of recruitment is shown in Supplementary Fig. 1. Of the K-DEPACS baseline sample ($n = 1,152$), 685 (59%) patients underwent the personality assessment at 12-weeks. Compared with the remainder of the sample, those assessed differed significantly in the following respects: younger age ($p = 0.012$), higher baseline HDRS score ($p < 0.001$), past history of depression ($p = .024$), hypercholesterolemia ($p = 0.004$), and lower Killip class ($p =$

0.01). Of these, 207 participated in the EsDEPACS trial (104 randomised to escitalopram and 103 to placebo); all were followed successfully for 24-weeks. There were no significant differences in any baseline characteristic including BFI scores between the two treatment groups. Of the 685 participants at baseline, 630 (92%) were followed at one year (369 with no depression, 84 on MTO, 87 on escitalopram, 90 on placebo). Of remaining 55 patients, 39 were lost to follow-up, 1 died, 11 refused to participate, and 4 were too unwell to participate. Attrition was significantly associated with the following baseline characteristics: older age ($p = 0.047$), higher baseline HDRS score ($p = 0.027$), lower troponin I ($p = 0.008$), and less hypercholesterolemia ($p = 0.009$).

Two personality types and baseline characteristics

Of the 685 patients, 406 (59.3%) were classified as resilient and 279 (40.7%) were classified as vulnerable. A comparison of the baseline characteristics of the two groups is presented in Table 1. The vulnerable group had a higher incidence of previous depression and history of ACS, as well as higher baseline HDRS scores, but there were no other significant differences between the two groups, aside from BFI score. There were significantly more patients with the resilient type in the no depression group than in the depression group (69.5% vs. 30.5%, $p < 0.001$), but there were no significant differences between the randomised groups of the EsDEPACS trial.

Treatment response at 24-weeks

HDRS score changes during the 24-week EsDEPACS trial were compared between the escitalopram vs. placebo groups and resilient vs. vulnerable personality types using mixed model RMANCOVA adjusted for all other baseline characteristics except BFI score, and are

summarised in Table 2 and Fig. 2. The HDRS score decreased significantly more in the escitalopram treatment group compared to placebo ($F = 7.68$, $p = 0.006$) and, independent of treatment group, more in patients with the resilient personality type compared with the vulnerable type ($F = 12.05$, $p < 0.001$). There was no significant interaction between personality type and treatment group.

Outcome at one year

The HDRS score changes at the one year follow-up were analysed similarly, as summarised in Table 3 and Fig. 3. The resilient personality type was associated independently and with a significantly greater decrease in HDRS score compared with the vulnerable type at one year ($F = 34.18$, $p = 0.001$). There was no significant interaction between personality type and the depression/treatment group.

Subgroup analysis according to depression diagnosis

Of the 207 patients who participated in the EsDEPACS trial, 92 (44.4%) were diagnosed with minor depression and 115 (55.6%) were diagnosed with major depression at baseline. Of the 630 patients who were followed-up after one year in the K-DEPACS trial, 119 (18.9%) were diagnosed with minor depression and 50 (7.9%) were diagnosed with major depression at baseline. The changes in HDRS scores at the 24-week and one year follow-ups in each subgroup were analysed similarly to the main analysis. In the minor depression subgroup, there was a significantly greater decrease in the HDRS scores of resilient-type versus vulnerable-type patients at 24-weeks ($F = 9.61$, $p = 0.003$) but no significant difference between treatment groups ($F = 1.18$, $p = 0.24$). In the major depression subgroup, there was a significantly greater decrease in the HDRS score of the escitalopram group compared to the

placebo group ($F = 4.70$, $p = 0.033$) but no significant difference between the two personality types ($F = 2.00$, $p = 0.16$). At one year, neither personality type nor treatment group had a significant influence on treatment response, nor was there a significant interaction between personality type and treatment group in either subgroup analysis at 24-weeks or one year.

Dimensional approaches

Results from the five dimensional scores are described in the Supplementary material and Supplementary table 1; these findings were similar to those obtained using the typological approach.. In the 24-week treatment response analyses, escitalopram and three personality dimensions (agreeableness, conscientiousness, and neuroticism) were independently associated with HDRS score at the trial end-point, but there were no significant interactions between personality dimensions and randomization group (all $p > 0.20$). Higher agreeableness and conscientiousness were associated with lower HDRS score, while higher neuroticism was associated with higher HDRS score at the trial end-point.

Similarly, in the one year outcome analyses, all personality dimensions apart from openness were independently associated with the HDRS score at the trial end-point, and there were no significant interactions between personality dimensions and the depression/treatment group (all $p > 0.10$). Higher extraversion, agreeableness, and conscientiousness were associated with lower HDRS score, while higher neuroticism was associated with higher HDRS score at the trial end-point.

Discussion

The principal findings of the investigation were that a vulnerable personality group could be identified from cluster analysis of FFM output which was independently associated with worse outcome of depression following ACS, both within a 24-week randomised controlled

trial and over a one year observational period, and independent of depression treatment allocation. Comparable findings were also observed for dimensional approaches of personality traits from the FFM. To the best of our knowledge, the present study is the first to use the full FFM personality inventory to investigate the treatment response and/or longitudinal course of depression in patients not only with ACS but also with any physical illnesses.

In personality research, dimensional approaches are quantitatively more informative than typological approaches, but translate poorly to individual patients (Costa et al., 2002), while typological approaches may be more useful in clinical settings. However, the replicability and utility of the FFM personality prototypes are still debated (Costa et al., 2002). In previous studies, two (Wardenaar et al., 2014, De Fruyt, 2002) or three clusters (Chapman and Goldberg, 2011, Berry et al., 2007) were replicated in various samples. In agreement with previous reports, we identified two personality clusters (resilient vs. vulnerable) in our sample. A two-cluster solution usually bifurcates the sample into groups which might be characterized as socially desirable vs. less desirable which, although coarse, has been suggested as useful in screening (De Fruyt, 2002). Other than the FFM personality types, the similarly bifurcated type D personality has received attention regarding the incidence and persistence of depression in cardiac patients (Denollet et al., 1995; Pedersen et al., 2006; Martens et al., 2008). However, the FFM typology offers a potentially more comprehensive approach. The vulnerable personality type in our study might well include the type D personality, as the concepts of 'negative affectivity' and 'social inhibition' in type D personality are consistent with the high neuroticism and low agreeableness in the vulnerable type from FFM (Denollet et al., 2005). Our results would help to integrate various opinions of previous personality researches in patient with ACS.

Although placebo-controlled trials have investigated the influence of FFM personality features on the treatment response to antidepressants, the results are controversial. A recent randomised controlled trial of patients with MDD found that personality predicted treatment outcome regardless of treatment type (Bagby et al., 2008; Thibodeau et al., 2015), but there was also a significant interaction in which personality predicted a differential response to treatment type (Bagby et al., 2008). Others have suggested that there is an interaction between the treatment outcome of paroxetine and neuroticism in MDD patients (Tang et al., 2009).

Differences in sample characteristics might be responsible for the discrepancy. Whereas approximately 60% of the participants were female in the previous study, more than 60% of the participants in the EsDEPACS study were male, which reflects the prevalence of ACS (Bagby et al., 2008; Thibodeau et al., 2015, Tang et al., 2009). These differences are important because the relationships between FFM personality and depression differ by gender (Fanous et al., 2007; Kendler and Gardner 2014). The vulnerable type may be associated with poor outcome because the FFM model of personality shares generic risk factors with depression (Kendler and Myers, 2010), which has a greater genetic overlap in men than women (Fanous et al., 2007). Next, it is possible that the participants of our study had some intensified personality characteristics compared to general populations, given longstanding suggestions of associations between personality traits and risk of coronary heart disease (Rosenman et al., 1976; Sirri et al., 2012). For example, type A behavior is more prevalent in patients with cardiovascular disease compared with other medical disorders (Sirri et al., 2012). Finally, the timing of the personality assessment could give rise to different results. In our study, personality traits were investigated 12-weeks after ACS and it is possible that responses might have been influenced by prior receipt of escitalopram. However, research on

the influences of selective serotonin reuptake inhibitors has yielded both positive (Tang et al., 2009; Du et al., 2002) and negative findings (Knorr et al., 2012; Jylhä et al., 2012). In our data, there were no significant differences between the escitalopram and placebo groups for either personality type.

Although there have been consistent reports of FFM personality influences on longitudinal course of depression in general populations from both typological or dimensional approaches of FFM (Wardenaar et al., 2014; Wiersma et al., 2011; Quilty et al., 2008), there has been no research investigating influences of the full five dimensions of FFM personality on longitudinal course in co-morbid depression with ACS. One published article investigated two selected dimensions of FFM, neuroticism and extraversion, and reported that pre-morbid neuroticism was a risk factor for depression (incidence and persistence) after somatic illness events, including myocardial infarction (de Jonge et al., 2006). Considering the FFM typological approach, there has been one published observational study of predictive value for treatment efficacy in MDD in primary care (Wardenaar et al., 2014). This classified MDD patients to vulnerable vs. resilient classes, and recovery was found to be slower in the vulnerable class. The results are in line with ours which vulnerable personality predict poor outcome. However, the previous study also reported a significant three-way interaction between personality class, time, and treatment allocation (Wardenaar et al., 2014), whereas we did not find an interaction between personality class and treatment allocation. There are important methodological differences between two studies. First, gender disparities may be important, as previously discussed, as about 70% of participants of the previous study were female (Wardenaar et al., 2014). Second, the previous study compared treatment groups receiving both pharmacotherapy and psychotherapy, whereas our comparison groups did not include psychotherapy. The role of personality might be treatment-specific; for example,

depressed patients with higher neuroticism were found to be more likely to respond to pharmacotherapy than psychotherapy (Bagby et al., 2008).

From a psychological perspective, characteristics of the resilient type could explain our results. Resilient personality type has been previously associated with a high level of ego-resiliency and a moderate standing on ego-control (Asendorpf et al., 1999). Ego-resiliency describes capacity to respond flexibly to changing situational demands, particularly stressful situations; ego-control refers to the capacity to constrain motivation and emotional impulses (Block et al., 1980). At the time of ACS diagnosis and treatment, resilient individuals may therefore more easily adapt to the stressful situation.

The subgroup analyses of the EsDEPACS trial revealed that only personality type significantly influenced treatment response in the minor depression subgroup, while only treatment type (escitalopram or placebo) significantly influenced treatment response in the major depression subgroup. The negative result of treatment type in the minor depression group was identical to the primary results of the EsDEPACS trial (Kim et al., 2015). These subgroup analyses also indicated that the influence of personality type was more significant in those with minor depression than in those with major depression. However, due to the small sample sizes in the subgroup analyses, and the negative results at the one year follow up, further studies are required to confirm these findings.

The present findings have some potential clinical implications. First, personality and escitalopram were independently and non-interactively associated with change in depressive symptoms over a 24-week period in depressed patients with ACS. In other words, escitalopram was effective in the treatment of depressive symptoms following ACS regardless of personality. Second, personality independently predicted the longitudinal course of depressive symptoms in patients with ACS. In particular, the vulnerable group – a cluster

characterized by higher neuroticism, lower extraversion, lower agreeableness, and lower conscientiousness – had worse long-term outcomes. The vulnerable personality group could be a target for potential interventions for reducing depressive symptoms, although the impact of such interventions requires further evaluation.

Strengths of the study included its prospective observational and interventional study design with large sample of ACS patients. The intervention was a double-blind randomised placebo-controlled trial. Participants were recruited at baseline consecutively from all eligible patients with a recent ACS and were followed at one year thereafter, which reduced the risk of error arising from heterogeneous examination times. With comprehensive human personality model of FFM, our results would help to integrate various opinions of previous personality researches in patient with ACS. Also, we analysed the influences of personality using both typological and dimensional approaches, maximizing output and allowing cross-testing of hypotheses.

Several limitations should be considered when interpreting the results. First, recruitment at a single institution may limit the sample generalisability; however, the single-center study has strengths in terms of consistency in the evaluation and treatment of patients. Second, personality traits were investigated 12-weeks after ACS as mentioned above. Third, of the 1,152 participants in the K-DEPACS cohort, only 685 (59%) were assessed for personality, and some baseline characteristics differed in analysed participants, which could have influenced the results. Fourth, the vulnerable group had a higher incidence of previous depression and ACS than the resilient group at baseline. Although these were considered as covariates, it should be borne in mind that the vulnerable personality was resulted in previous depression or ACS (scar effect) (fanous et al., 2007). However, the scar effect of previous depression on current personality is still debated hypothesis (fanous et al., 2007, Jylhä et al.,

2009). Similarly, although the baseline HDRS scores were included as covariates in the RMANCOVA, we also couldn't exclude the effect of baseline depressive mood on personality characteristics (state effect) (Jylhä et al., 2009) because the baseline HDRS score was higher in the vulnerable group than that in the resilient group. However, in previous longitudinal study, the level of neuroticism and extraversion were still differ between depressive patients and the general population, after controlling depression and excluding state effect. Thus, FFM personality features have a trait effect on depression (Jylhä et al., 2009). Finally, although the FFM typological approach gave clear potentially clinically relevant findings, replication of the prototype remains a critical objective. Although they have potential clinical utility for screening, dimensional approaches have been found to be consistently better predictors of ego resiliency and control (Costa et al., 2002).

In conclusion, personality influences the longitudinal course of depression in ACS patients independent of treatment allocation. Escitalopram was effective in the treatment of depressive symptoms following ACS regardless of personality. Further clinical trials should assess treatment response to other antidepressants in depressed patients with ACS according to personality characteristics.

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Fig. 1. Personality profile clusters according to Big Five Inventory z-scores (n = 685).

Fig. 2. Changes in the Hamilton Depression Rating Scale (HDRS) score over 24-weeks according to treatment status and personality cluster (n = 207). The results were obtained using repeated measures analysis of covariance in a mixed model with the corresponding baseline HDRS scores, age, gender, education, history of depression, hypertension, diabetes, current smoking, obesity, hypercholesterolemia, personal and family history of acute coronary syndrome, diagnosis of acute coronary syndrome, Killip class, ejection fraction, and levels of creatinine kinase-MB and troponin I. Significant differences in time \times group and time \times personality type interactions were found on all outcomes ($p = 0.006$ and $p < 0.001$, respectively).

Fig. 3. Changes in the Hamilton Depression Rating Scale (HDRS) score over one year according to depression diagnosis, treatment status, and personality cluster (n = 630). The results were obtained using repeated measures analysis of covariance in a mixed model with the corresponding baseline HDRS scores, age, gender, education, history of depression, hypertension, diabetes, current smoking, obesity, hypercholesterolemia, personal and family history of acute coronary syndrome, diagnosis of acute coronary syndrome, Killip class, ejection fraction, and levels of creatinine kinase-MB and troponin I. Significant differences in time \times group and time \times personality type interactions were found for all outcomes ($p < 0.001$, both).

Table 1. Baseline characteristics by personality cluster

	Total	Personality cluster		<i>p</i>
		Resilient	Vulnerable	
	(n = 685)	(n = 406)	(n = 279)	
Demographic factors				
Age, mean (SD), years	57.9 (11.0)	58.5 (10.7)	57.0 (11.4)	0.084
Female gender, n (%),	202 (29.5)	112 (27.6)	90 (32.3)	0.19
Education, mean (SD), years	9.9 (4.5)	9.6 (4.7)	10.2 (4.3)	0.10
Psychological factors				
HDRS score, mean(SD)	8.23 (6.4)	6.6 (5.8)	10.7 (6.5)	< 0.001
Previous depression, n (%)	32 (4.7)	13 (3.2)	19 (6.8)	0.03
Extraversion, mean (SD)	3.0 (0.5)	3.2 (0.5)	2.8 (0.4)	< 0.001
Agreeableness, mean (SD)	3.7 (0.5)	4.0 (0.3)	3.4 (0.44)	< 0.001
Conscientiousness, mean (SD)	3.7 (0.5)	3.9 (0.4)	3.3 (0.4)	< 0.001
Neuroticism, mean (SD)	2.7 (0.6)	2.3 (0.4)	3.2 (0.4)	< 0.001
Openness, mean (SD)	2.9 (0.6)	2.8 (0.6)	2.9 (0.5)	0.58
Cardiac risk factors				
Hypertension, n (%)	327 (47.7)	183 (45.1)	144 (51.6)	0.09
Diabetes mellitus, n (%)	151 (22.0)	89 (21.9)	62 (22.2)	0.93
Hypercholesterolemia, n (%)	364 (53.1)	211 (52.0)	153 (54.8)	0.46
Obesity, n (%)	297 (43.4)	170 (41.9)	127 (45.5)	0.34
Current smoker, n (%)	258 (37.7)	153 (37.7)	105 (37.6)	0.99
Previous history of ACS, n (%)	35 (5.1)	15 (3.7)	20 (7.2)	0.04
Family history of ACS, n (%)	22(3.2)	12 (3.0)	10 (3.6)	0.65
Current cardiac status				
ACS diagnosis, n (%)				0.58
Myocardial infarction	494 (72.1)	296 (72.9)	198 (71.0)	
Unstable angina	191 (27.9)	110 (27.1)	81 (29.0)	
Killip class > 1, n (%)	106 (15.5)	56 (13.8)	50 (17.9)	0.14
LVEF, mean (SD), %	60.8 (11.3)	60.4 (11.5)	61.3 (10.9)	0.30
Troponin I, mean (SD), mg/dL	9.2 (13.8)	8.5 (13.4)	10.2 (14.3)	0.12
CK-MB, mean (SD), mg/dL	16.7 (36.7)	16.1 (34.0)	17.6 (40.4)	0.61

ACS, acute coronary syndrome; CK-MB, creatinin kinase-MB; HDRS, Hamilton Depression

Rating Scale; LVEF, left ventricular ejection fraction; SD, standard deviation.

Table 2. Effects of medication and personality in a 24-week double-blind trial on Hamilton Depression Rating Scale scores of patients with acute coronary syndrome (n = 207)

	HDRS, mean (SD)		F	p^a	Post hoc
	At baseline	24-weeks			
Time	15.6 (4.7)	9.3 (6.0)	2.48	0.12	-
Time x Randomization group			7.68	0.006	-
Depression on escitalopram	15.9 (5.0)	8.5 (6.1)			
Depression on placebo	15.2 (4.4)	10.2 (5.8)			
Time x Personality type			12.05	< 0.001	-
Resilient	15.1 (4.3)	7.5 (5.5)			
Vulnerable	15.9 (4.9)	10.6 (6.0)			
Time x Group x Personality type			< 0.01	0.97	N.S.

HDRS, Hamilton Depression Rating Scale; SD, standard deviation.

^a Repeated-measures analyses of covariance, adjusted for all variables.

Table 3. Effects of depression, treatment status, and personality on one year outcomes of patients with acute coronary syndrome (n = 630)

	HDRS, mean (SD)		F	p^a	Post hoc
	At base	One year			
Time	8.0 (6.3)	6.0 (5.4)	7.25	0.007	-
Time x Group			11.39	< 0.001	
No depression (N)	3.7 (2.6)	4.1 (4.3)			M < N,E,P & E > P
Depression on MTO (M)	11.3 (3.6)	10.0 (5.7)			
Depression on escitalopram (E)	15.7 (4.9)	7.1 (5.6)			
Depression on placebo (P)	15.2 (4.4)	8.9 (5.2)			
Time x Personality type			34.18	< 0.001	
Resilient	6.4 (5.6)	4.4 (4.2)			-

Vulnerable	10.5 (6.4)	8.4 (6.0)	-	
Time x Group x Personality type			.02	0.99
				N.S.

HDRS, Hamilton Depression Rating Scale; MTO, medical treatment only; SD, standard deviation

^aRepeated-measures analyses of covariance, adjusted for all variables.

Highlights

- Vulnerable personality is related with poor outcome of depression in ACS.
- Vulnerable personality characterized by low E,A,C but high N in ACS.
- Personality influences on depression independent of antidepressant treatment.
- Personality independently predicts the longitudinal course of depression in ACS.
- A Single site recruitment and the time of personality assessment are limitations.

Fig. 1. Personality profile clusters according to Big Five Inventory z-scores (n = 685).

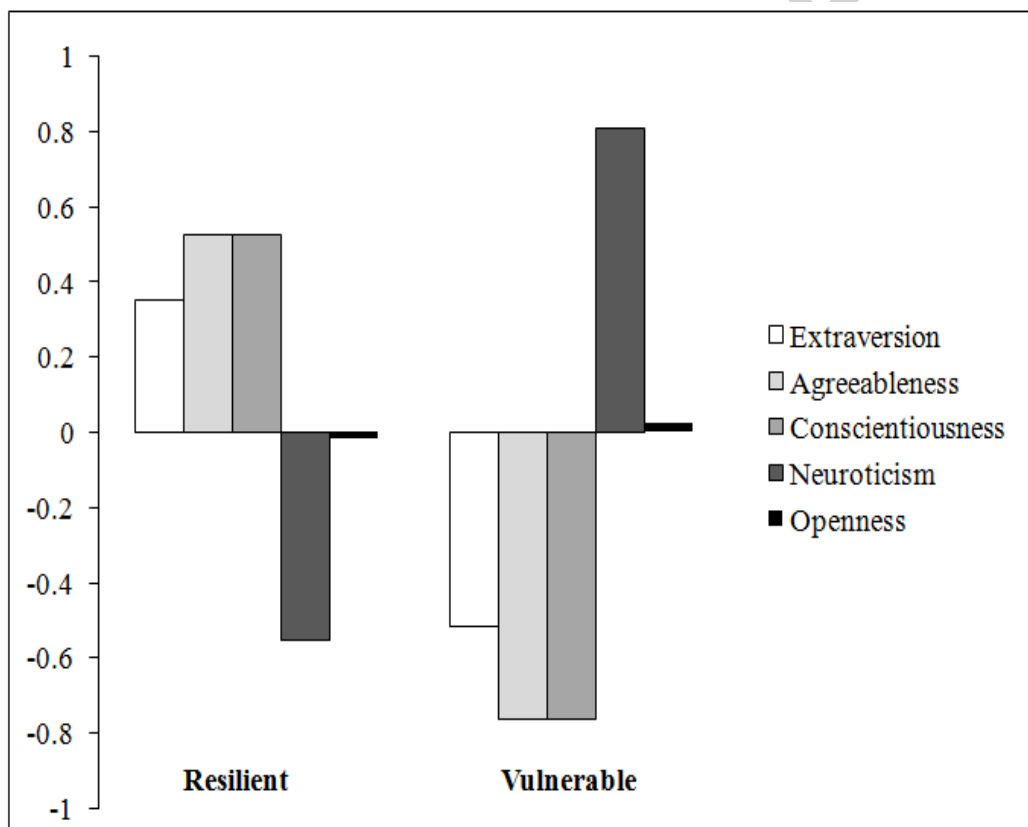


Fig. 2. Changes in the Hamilton Depression Rating Scale (HDRS) score over 24-weeks according to treatment status and personality cluster ($n = 207$). The results were obtained using repeated measures analysis of covariance in a mixed model with the corresponding baseline HDRS scores, age, gender, education, history of depression, hypertension, diabetes, current smoking, obesity, hypercholesterolemia, personal and family history of acute coronary syndrome, diagnosis of acute coronary syndrome, Killip class, ejection fraction, and levels of creatinine kinase-MB and troponin I. Significant differences in time \times group and time \times personality type interactions were found on all outcomes ($p = 0.006$ and $p < 0.001$, respectively).

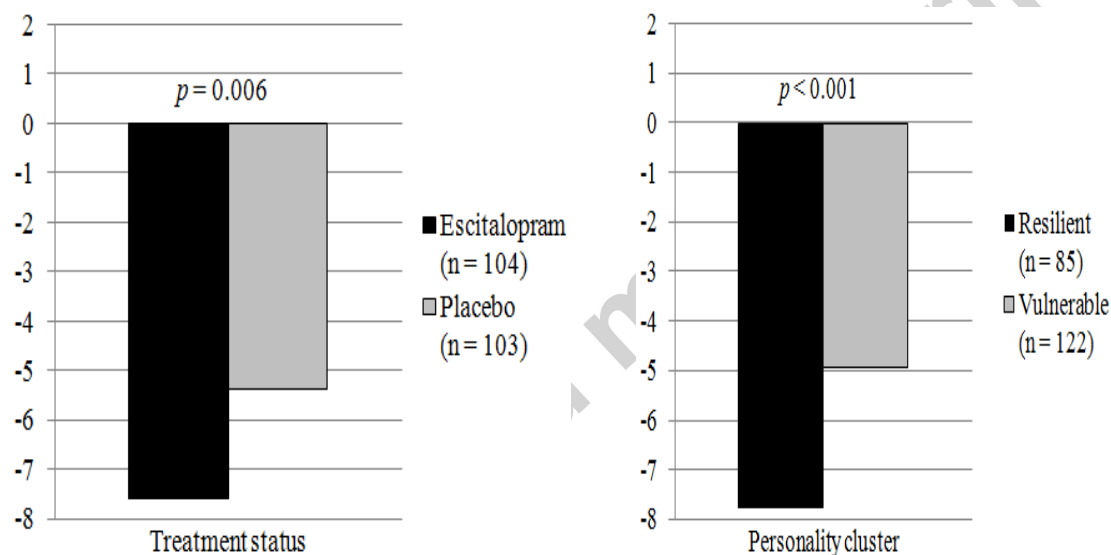


Fig. 3. Changes in the Hamilton Depression Rating Scale (HDRS) score over one year according to depression diagnosis, treatment status, and personality cluster ($n = 630$). The results were obtained using repeated measures analysis of covariance in a mixed model with the corresponding baseline HDRS scores, age, gender, education, history of depression, hypertension, diabetes, current smoking, obesity, hypercholesterolemia, personal and family

history of acute coronary syndrome, diagnosis of acute coronary syndrome, Killip class, ejection fraction, and levels of creatinine kinase-MB and troponin I. Significant differences in time \times group and time \times personality type interactions were found for all outcomes ($p < 0.001$, both).

